REMARKS

Claims 1-16, 21, 22, 25-27, 42, 43 and 46-69 are pending in the present application, the Examiner having withdrawn claims 17-20, 23, 24, 28-41, 44 and 45 from consideration as drawn to a non-elected invention. By this amendment Claims 2, 15, 16 and 66 have been canceled without prejudice to renewal of prosecution of the subject matter encompassed by the claims in a related copending application. Further, claims 1, 6, 9, 11, 21, 22, 25, 27, 42, 43, 46, 49, 50-53, and 55-57 have been amended as set forth in detail below. Also, claim 70 has been added to specifically recite a particular embodiment of the present invention where the chimeric peptide comprises three subregions including helper T cell activating epitopes, cytotoxic T cell epitopes and neutralizing epitopes of the organism for which a cytotoxic T cell and an antibody immune response is desired. Support for this new claim can be found in the specification at, for example, page 14, lines 27-34 and page 16, lines 17-31. All amendments to the claims and the newly added claims are fully supported by the specification and no new matter has been added.

The Examiner has deemed restriction for substantive examination of the present application proper for an invention limited to only claims directed to the administration of a single peptide (SEQ ID NO:2) for inducing an antigen specific rectal mucosal cytotoxic T cell response in a mammalian subject and to compositions containing that peptide. Applicants strongly object to the decision by the Examiner to make the restriction final and respectfully request the Examiner to reconsider. Applicants believe that the general policies of the Patent and Trademark Office for restriction of the claims in a patent application and the ability of an applicant to claim and protect their invention fully have not been properly balanced in the present application. The Examiner by not allowing Applicants to prosecute claims directed to even methods comprising administration of a limited number of chimeric peptides from a single virus with the particular claimed characteristics to the rectal mucosa to induce an antigen specific rectal mucosal cytotoxic T cell response as was proposed in the first request for restriction prevents the prosecution of claims that would provide a reasonable scope of protection for the present invention. Instead, Applicants must pursue methods for the administration of each specifically described peptide in a separate patent application with no opportunity for more

generic protection for the methods and compositions of the present invention. Applicants do not believe this outcome embodies the intent of Patent Office restriction practice.

The methods of the present invention are not believed to be limited to only the single example to which the invention has been limited, but are directed to the administration of a chimeric peptide comprising the helper T cell activating epitopes and cytotoxic T lymphocyte epitopes of any organism or cell to which a systemic and rectal mucosal CTL response is desired. Chimeric peptides containing helper T cell activating epitopes and cytotoxic T lymphocyte activating epitopes of HIV-1 are specifically described and enabled by the present application. These chimeric peptides can be constructed with helper T cell activating and cytotoxic T lymphocyte activating epitopes of known isolates of HIV-1. Epitopes as defined in the present invention are specifically provided for the IIIB isolate and MN isolates of HIV-1. These two isolated are known to be associated with the majority of the infections in North American and Europe. Therefore, Applicants strongly disagree with the Examiner that consideration of methods for administering a chimeric peptide limited to a single virus comprising T helper epitopes and cytotoxic T cell epitopes of, for example HIV-1, as set forth in the first request for restriction, places an undue burden on the Examiner to search and examine the present invention. It is respectfully requested that the Examiner reconsider the restriction of the claims in the present application to a simple peptide.

The Examiner has also indicated that the present application when filed did not contain an abstract of the disclose on a separate sheet as required by 37 C.F.R. § 1.72(b). An abstract on a separate sheet has been requested. Applicants respectfully submit that the present application is a United States national phase application of PCT US/98/19028 filed under 35 U.S.C. § 371 with the Receiving Office of the United States Patent and Trademark Office on September 11, 1998 and published as WO 99/12563. As a convenience a copy of the PCT publication and other communications were submitted with the request for entering the national phase in the United States March 9, 2000. Applicants believe that the record copy of the International application as filed should have been forwarded to the Examiner by the United States Receiving Office. To further expedite prosecution of the subject application, a copy of the abstract filed with the Receiving Office September 11, 1998 is attached hereto along with a copy

of the return receipt post card. Applicants submit that the present application was properly filed with an abstract as required under 37 C.F.R. § 1.72(b).

Rejections Under 35 U.S.C. § 112, Second Paragraph:

Claims 49 and 55 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner does not believe the team "rectal emulsion" is clear and distinguishable from any other emulsion. Further, the Examiner does not appear to understand what Applicants mean by the term "base material" in claim 55.

Applicants have amended claim 49 to recite that the immunogenic composition is "formulated" as a rectal emulsion or gel preparation. Such formulations adapted for rectal mucosal administration are described at, for example, pages 21 through 24. Rectal emulsion vehicles are disclosed specifically at page 21, lines 31 through 33. Gel preparations suitable for formulating compositions for rectal administration are specifically described at, for example, page 21, lines 33 through 37. Further, claim 55 has been amended to recite dependency on claim 54 in order to provide antecedent basis for the term "base material." Base materials as used in the present invention are fully defined at, for example, pages 21 through 24. Specifically, various base materials are defined at, for example, page 22, lines 1 through 18. Base materials can include, for example, a conventional suppository base material, a lipophilic base material, or a hydrophilic base material. In addition specific examples of various base materials are set forth, at for example, page 22, lines 4 through 18.

As set forth in the above remarks Applicants believe that the terms "rectal emulsion" and "base material" are set forth with sufficient particularity in the currently pending claims to be considered definite under 35 U.S.C. § 112, second paragraph. It is respectfully requested that the Examiner reconsider and withdraw the present rejection.

Rejections Under 35 U.S.C § 101:

Claims 1-16, 21, 22, 25-27, 42 and 43 stand rejected under 35 U.S.C. § 101, the Examiner believing the claimed invention is not supported by either a credible asserted utility or a well established utility. In particular, the Examiner has focused on statements in the specification that one can use the claimed invention as a vaccine. It is the belief of the Examiner that the specification fails to teach such a use, nor does the Examiner believe that the specification describes the use of a HIV vaccine. Further, the Examiner has listed what the Office believes are the well known difficulties "inherent" to the development of an HIV vaccine, including:

"1) the extensive genomic diversity associated with the HIV retrovirus";

"2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form;"

"3) the existence of latent forms of the virus; (i.e., beyond blood-brain barrier);

5) the complexity and variation of the elaboration of the disease; and

6) the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences."

Because of these factors, the Examiner believes that one of ordinary skill in the art is prevented from accepting any vaccine or immunization treatment or any therapeutic regimen on its face given the intense interest in developing HIV vaccines and the lack of success in doing so. Further, the Examiner believes either clinical or art accepted *in vivo* or *in vitro* data, or a combination of these must be provided in order to provide proof of utility with regard "to drugs and their uses." Any data provided must convince the Examiner that it would be sufficient for one of ordinary skill in the art to believe for the proposed utility to be established.

Applicants traverse the rejection of the Examiner generally rejecting methods for the immune stimulation of a mammalian subject to increase the subjects ability to kill or reduce the proliferation of HIV as lacking in a credible utility or lacking a well established utility. Also, in order to further expedite prosecution of this application and in light of the Examiner's decision to limit the subject matter of the claims under examination in this application to methods of

administering a single chimeric peptide from one HIV-1 isolate the claims have been amended in order to point out the invention with greater particularity.

In particular, claim 1 has been amended to recite a method for inducing an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response in a mammalian subject comprising contacting a rectal mucosal tissue of the subject with a composition comprising a chimeric peptide containing a first subregion with multiple overlapping helper T cell activating epitopes of a HIV isolate that can be presented by multiple MHC class II molecules and a second subregion with a CTL activating epitope of the HIV isolate, wherein the contacting induces an antigen specific systemic and rectal mucosal CTL response that can kill or reduce the proliferation of a virus expressing the CTL activating epitope of the HIV isolate. Support for this amendment can be found, for example, at page 13, line 25 through page 17, line 31. Also, the methods elected with traverse in the prior response are limited to the chimeric peptide designated SEQ ID NO:2, *HIV-1* CLUVAC PCLUS3-18IIIB. This peptide comprises overlapping helper T cell activating epitopes as depicted in SEQ ID NO: 18 and the CTL activating epitope of HIV-1 isolate IIIB depicted in SEQ ID NO: 15. The peptide of SEQ ID NO: 15 also includes a primary neutralizing domain of HIV-1 isolate IIIB specifically recited as the third subregion of the chimeric peptide of new claim 70. Applicants believe that the claimed invention as originally filed and particularly as set forth in the amended claims provided herein are supported by a credible asserted utility or a well established utility as required by 35 U.S.C. § 101.

As an initial matter Applicants object to the Examiner focusing on only the disclosed use of the claimed invention as a "vaccine" in making this rejection and not providing any reasoning or evidence how these difficulties in finding a clinically effective HIV "vaccine" relate to the present invention as restricted and claimed. The various reasons set forth by the Examiner why "vaccine" methods for HIV are not taught or described by the specification are not believed to be directed to the claimed methods as restricted by the Examiner or as set forth by currently pending claims 1-16, 21, 22, 25-27, 42 and 43. It should be noted that claims 2, 15, and 16 have been canceled without prejudice to renewal of prosecution of the subject matter encompassed by the claims in this or a related copending application and that claims 1, 6, 9, 11,

21, 22, 25, 27, 42, 43 have been amended to set forth the present invention with greater particularity.

The first reason set forth by the Examiner that the claimed invention is not supported by a credible or well established utility is that HIV is known to possess extensive genomic diversity. The claims of the present invention as restricted and as currently amended are directed to methods comprising administering intrarectally a chimeric peptide that comprise defined regions of HIV. The first region comprises a subregion with multiple overlapping helper T cell activating epitopes of an HIV-1 isolate that can be presented by multiple MHC class II molecules and the second subregion comprises a CTL activating epitope of the HIV-1 isolate. Each of the subregions contribute to the production of antigen specific systemic and rectal mucosal CTL response specific to the HIV-1 isolate when the compositions are administered directly to the rectal mucosa. The existence of genomic variability of HIV does not detract from the utility of the claimed invention to induce an antigen specific systemic and rectal CTL response because the response is specific to the particular HIV-1 isolate containing the epitopes. It is well known to the skilled artisan that the induction of a CTL response is critical to treatment of or protection from HIV infection. A CTL response to even a single isolated of HIV can be of great utility to the medical community.

Further, the specification provides guidance such that the skilled artisan can expand the CTL response to additional isolates of HIV-1 by the administration of other chimeric peptides with subregions comprising a CTL activating epitope from other known or discovered HIV isolates. For example, as disclosed in the present application a chimeric peptide containing a first subregion with multiple overlapping helper T cell activating epitopes from the HIV-1 isolate IIIB that can be presented by multiple MHC class II molecules and a subregion with a CTL activating epitope of the HIV-1 isolates HIV IIIB and HIV MN can be administered to the rectal mucosal. Administration of either composition was found to induce an antigen specific systemic and rectal CTL response. While administration of the chimeric peptide of SEQ ID NO:2 was found to induce not only the antigen specific CTL response, but also was found to induce a CTL response that killed or prevented the proliferation of a recombinant vaccinia virus that expressed the gp160 envelope protein of HIV-1 isolate IIIB. Therefore, the amino acid sequence variability of certain HIV isolates does not provide evidence that the claimed methods

of the present invention are not supported by an asserted credible or well established utility. Further, the invention also describes methods for inducing a systemic and rectal antigen specific CTL responses to other viruses, bacteria, protozoa or even tumor cells by administering chimeric peptides with helper T cell activating epitopes and CTL activating epitopes from the antigen to which a response is desired.

The second issue raised by the Examiner is the transmission of virus from cell to cell by certain mononuclear cells. Contrary to the opinion of the Examiner cell to cell transmission of HIV does not suggest that the pending claims of the present invention lack an asserted credible or well established utility, but instead provides evidence why the claimed methods are supported by a credible or well establish utility. The pending claims are directed to methods for the induction of an antigen specific systemic and rectal mucosal CTL response. Whether cell to cell transmission of HIV would be expected or not during infection does not effect the ability of the methods and compositions of the present invention to induce the response claimed. In fact, one of skill in the art would expect the induction of an antigenic specific systemic and rectal mucosal CTL response to be particularly useful in eliminating many infected cells.

The Examiner has also noted the existence of latent forms of the virus (*i.e.*, beyond the blood-brain barrier) in some individuals with HIV infection. Applicants do not believe that the Examiner has provided any particular reason or evidence why the presence of latent forms of HIV would indicate that the claimed methods to induce an antigen specific systemic and rectal mucosal CTL response is not supported by a credible or well established utility. Applicants believe that the methods of the present invention are particularly useful because the methods induce an antigen specific CTL response in the rectal mucosa. The rectal mucosa is now known to be a major reservoir for HIV virus and that the killing of or any reduction in the proliferation of HIV in the rectal mucosa is very important in the treatment of HIV infection.

The complexity and variation of the elaboration of the disease associated with HIV infection has also been suggested by the Examiner to demonstrate that the present invention is not supported by a credible or well established utility. Again, Applicants do not believe the Examiner has provided any specific reasoning or references to support why the complexity or

variation of the elaboration of the disease associated with HIV infection demonstrates that the induction of an antigen specific systemic and rectal mucosal CTL response that can kill or reduce the proliferation of a virus expressing the cytotoxic T cell epitope of the HIV isolate contained in the chimeric peptide used in the methods claimed is not supported by a credible or well established utility. It is clear that the skilled artisan understands the clinical significance of the induction of both a CTL and immune response in the rectal mucosa to assist in the treatment of HIV infection. The methods of the invention provide for the first time evidence of a reduction in the proliferation or killing against mucosal viral challenge mediated by cytotoxic T cells in the rectal mucosa. The induction of such a response can inhibit proliferation or kill virus which is known to be critical to any treatment for HIV infection.

The Examiner has also raised the issue of the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences. Applicants do not believe that the Examiner has properly made the rejection on this basis. As above, this basis for rejection is merely a general statement and is not directed specifically toward any peptide that might described in the present application or that would be encompassed by the pending claims. The claimed methods are directed to particular portions of HIV having helper T cell activating epitopes and CTL activating epitopes and no reasoning or reference has been provided by the Examiner to indicate or suggest that these well defined regions have been associated with immunosuppression or any other detrimental consequence. Therefore, Applicants do not believe this general assertion can be used to question the support of the pending claims as having a credible or established utility.

Further, although Applicants believe the claims pending in the application are fully supported by either a credible asserted utility or a well established utility the following article (Belyakov *et al.*, *Nature Med.* 7:1320-1326) published by Applicants and others subsequent to the filing of the present application is provided. The methods described in the publication as disclosed in the present application provide for the intrarectal administration of chimeric peptides that comprise a first subregion having helper T cell activating epitopes and CTL activating epitopes. Specifically, Belyakov *et al.* the helper T cell activating epitopes were those designated SEQ ID NO: 18 and the first 27 amino acids of SEQ ID NO: 12 in the present application. While the CTL activating epitopes were derived from simian immunodeficiency

virus (SIV) Gag and Pol presented by the rhesus major histocompatibility (MHC) class I molecule, Mamu-A*01 as a replacement for the HIV cytotoxic T cell epitope within the P18 subregion of the peptide.

The results presented by Belyakov *et al.* demonstrate that intrarectal immunization of rhesus monkeys with the chimeric peptides induced a systemic and rectal CTL response specific to the CTL epitopes of the chimeric peptide. Further, it was demonstrated that rectal administration of the chimeric peptides provided partial protection against mucosal challenge with a pathogenic hybrid simian/human immunodeficiency virus (SHIV). The SHIV expressed HIV-1 gp160, including the helper epitopes, and SIV Gag and Pol proteins, including the CTL epitopes of the chimeric peptides. The protection provided by the chimeric peptides was considered partial because in the monkeys administered the chimeric peptides and challenged with SHIV were found to become infected initially, but then rapidly cleared the infection. The animals remained free of infection and free of signs of disease, maintaining a stable CD4 count for the duration of the study. Control animals showed persistent viremia, falling CD4 counts and symptoms of disease. Thus, the methods of the present invention administering a chimeric peptide composition comprising a first subregion with multiple overlapping helper T cell activation epitopes of a HIV isolate that can be presented by multiple MHC class II molecules and a second subregion with a CTL activating epitope of a SIV isolate can induce an antigen specific CTL response that can kill or reduce the proliferation of a virus expressing the SIV CTL activating epitope.

These results demonstrate that not only can the methods of the present invention using chimeric peptides having a cytotoxic T cell epitope of HIV1 isolate IIIB induce an antigen specific systemic and rectal mucosal CTL response when administered intrarectally, but also that chimeric peptides having the same helper T cell epitopes and having cytotoxic T cell epitopes derived from other related retroviruses can be used in the place of the cytotoxic T cell epitope of HIV-1 in the claimed methods and still induce the effect taught by the specification as filed. These data provide additional evidence using an animal model of immunodeficiency virus infection accepted by those of ordinary skill in the art that the methods of the present invention are supported by either an asserted credible utility or a well established utility.

Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-16, 21, 22, 25-27, 42 and 43 under 35 U.S.C. § 101 in view of the amendments to the claims and the above remarks.

Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 1-16, 21, 22, 25-27, 42, and 43 stand rejected under 35 U.S.C. § 112, first paragraph, the Examiner believing that as the claimed invention is not supported by either a credible asserted utility or a well established utility as set forth above in the rejection under 35 U.S.C. § 101 one skilled in the art would not know how to use the claimed invention.

Applicants traverse this rejection and direct the Examiner to the response above which provides evidence and argument that the presently claimed invention is fully supported by either a credible asserted utility or a well established utility. The skilled artisan is provided detailed methods for administering the chimeric peptides of the present invention intrarectally to induce an antigen specific systemic and rectal mucosal CTL response that can kill or reduce the proliferation of a virus expressing the cytotoxic T cell epitope of the chimeric peptide. Therefore, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-16, 21, 22, 25-27, 42, and 43 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102:

Claims 46-48, 59 and 66 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Ahlers *et al.* (*J. Immunol.* 150:5647-5665 (1993); IDS Ref. AH). The Examiner believes that as the preamble of the claims is not accorded significant patentable weight as it only describes an intended use, Ahlers *et al.* teaches immunogenic peptide compositions comprising SEQ ID NO:2 (PCLUS 1-18). The Examiner also believes that the reference teaches the administration of the composition with an adjuvant and that the composition can be "installed in the rectum as an enema."

Without acquiescing to the rejection or any comment of the Examiner, Applicants have amended claims 46, 48-53, 55 and 56 to further expedite prosecution of certain embodiments of the invention without prejudice to prosecuting any of the subject matter believed to be limited from the pending claims in a related co-pending application. In particular, claim 46

has been amended to recite an immunogenic composition comprising a chimeric peptide containing a first subregion with multiple overlapping helper T cell activating epitopes from an HIV isolate that can be presented by multiple MHC class II molecules and a second subregion with a CTL activating epitope from the HIV isolate, formulated for intrarectal delivery to the rectum, colon, sigmoid colon, or distal colon that induces an antigen specific systemic and rectal mucosal CTL response that can kill or reduce the proliferation of a virus expressing the cytotoxic T cell epitope. Claims 47, 49-53, 55 and 56 have been amended to be consistent with amended claim 46.

Applicants believe that the amendments to claim 46 obviates the rejection of claims 46-48, 59 and 66 as anticipated by Ahlers *et al.* as the reference does not disclose or suggest each element of the amended claims. In particular, Ahlers *et al.* discloses the use of intraperitoneal administration of a chimeric peptide containing a helper T cell activation epitope of HIV-1 and an epitope that induces an antibody response specific for HIV-1. Certain of the peptides are encompassed by the pending claims, but were intended for the induction of an antigen specific systemic antibody response. The reference suggests the use of the disclosed peptide to possibly induce a CTL response because the chimeric peptide also contains a CTL activating epitope, but no guidance is provided for how the composition would be formulated or for the mode of administration to induce a CTL response. Further, the reference does not speculate on the tissue specificity of the induction of the CTL response such as, rectal mucosal, lymph nodes, spleen, or systemic. Prior to the present invention little was known about the induction of a CTL response in the rectal mucosa with a nonliving vaccine, or about the efficacy of the induced CTL response against mucosal challenge. (See, Belyakov *et al.*, *Proc. Natl. Acad. Sci. USA* 95:1709-1714 (1998) at page 1709, right column; Reference AL of the IDS). Therefore, no disclosure or motivation is provided by Ahlers *et al.* for the formulation of the compositions of the present invention for administration to the rectal mucosa.

In view of the amendments to the claims and the remarks above Applicants respectfully request the Examiner to reconsider the rejection of claims 46-48, 59 and 66 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Ahlers *et al.*

Rejections Under 35 U.S.C. § 103:

Claims 46 through 69 stand rejected under 35 U.S.C. § 103(a) the Examiner believing the claims are obvious over Ahlers *et al.* in view of admissions of the specification. In particular, the Examiner describes Ahlers *et al.* as teaching the immunogenic peptide compositions comprising SEQ ID NO: 2, but that it does not explicitly teach the numerous specific adjuvants of the present invention. The Examiner believes that these adjuvants are known in the art as exemplified in the specification. It is the belief of the Examiner that it would have been within the skill of the ordinary artisan at the time the invention was made to modify the antigenic peptide disclosed by Ahlers *et al.* with known carriers, adjuvants, etc., with the expectation of optimizing its use as an immunogen. The Examiner has also cited certain parts of the specification as filed as teaching that various adjuvants useful in mucosal formulations, as well as rectal delivery formulations were known at the time of filing the present application.

Applicants respectfully traverse this rejection. In particular, the Examiner has not provided any motivation to combine the fact that rectal delivery formulations were known in the art with the delivery of soluble chimeric peptide antigens having overlapping helper T activating epitopes and cytotoxic T cell activating epitopes to the rectal mucosa. Ahlers *et al.* teach the administration of the disclosed peptides intraperitoneally and suggest that the peptides might be administered by an alternate route and using different adjuvant formulations to elicit both an antibody response and a CTL response, there is no suggestion that the peptides be formulated for administration directly to the rectal mucosa. As above, prior to the work of Applicants' little was known about approaches to induce a CTL response in the mucosa with a non-living vaccine composition. Therefore, Applicants do not believe the Examiner has provided any motivation for combining the peptides of Ahlers *et al.* used for systemic administration to induce a systemic antibody response with any formulation known for direct administration to the rectal mucosa including any formulations using adjuvants or other additives specialized for rectal pharmaceutical formulations such that the present composition claims. Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 46-69 as obvious over Ahlers *et al.* in view of the specification.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 30 January 2003

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APPENDIX

Version With Markings to Show Changes Made

IN THE CLAIMS:

1. (Amended) A method for inducing [a protective] an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte (CTL) response in a mammalian subject comprising contacting a rectal mucosal tissue of the subject with a composition comprising a [purified soluble antigen] chimeric peptide containing a subregion with multiple overlapping helper T cell activating epitopes of a HIV isolate that can be presented by multiple MHC class II molecules and a subregion with a CTL activating epitope of the HIV isolate, wherein the contacting induces an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response that can reduce the proliferation of a virus expressing the CTL activating epitope of the HIV isolate.

6. (Twice Amended) The method of claim 5, wherein the cytokine is contacted with [a] the rectal mucosal surface of the subject.

9. (Amended) The method of claim 8, wherein the purified interferon-γ is [a] the rectal contacted with a mucosal surface of the subject.

11. (Amended) The method of claim 10, wherein the purified interferon-γ is contacted with a mucosal surface of the subject.

21. (Amended) The method of claim 1, wherein the [antigen is a] chimeric peptide [comprising an *HIV-1* cluster peptide vaccine construct (CLUVAC) selected from the group consisting of] comprises:

EQMHEDIISLWDQSLKPCVKRIQRGPGRAFVTIGK (SEQ ID NO.: 1)

KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK (SEQ ID NO: 2)

RDNWRSELYKYKVVKIEPLGVAPTRIQRGPGRAFVTIGK (SEQ ID NO: 3)

AVAEGTDVIEVVQGAYRAIRHIPRRIRQGLERRIQRGPGRAFVTIGK (SEQ ID NO: 4),

DRVIEVVQGAYRAIRHIPRRIRQGLERRIQRGPGRAFVTIGK (SEQ ID NO: 5),

DRVIEVVQGAYRAIRRIQRGPGRAFVTIGK (SEQ ID NO: 6),

AQGAYRAIRHIPRRIRRIQRGPGRAFVTIGK (SEQ ID NO: 7),

EQMHEDIISLWDQSLKPCVKRIRIHIGPGRAFYTTKN (SEQ ID NO: 8),

KQIINMWQEVGKAMYAPPISGQIRRIHIGPGRAFYTTKN (SEQ ID NO: 9),

RDNWRSELYKYKVVKIEPLGVAPTRIHIGPGRAFYTTKN (SEQ ID NO: 10),

AVAEGTDVIEVVQGAYRAIRHIPRRIRQGLERRIHIGPGRAFYTTKN (SEQ ID NO: 11),

DRVIEVVQGAYRAIRHIPRRIRQGLERRIHIGPGRAFYTTKN (SEQ ID NO: 12),

DRVIEVVQGAYRAIRRIHIGPGRAFYTTKN (SEQ ID NO: 13), or

AQGAYRAIRHIPRRIRRIHIGPGRAFYTTKN (SEQ ID NO: 14).

22. (Amended) The method of claim 21, wherein the [*HIV-1* CLUVAC] chimeric peptide is *HIV-1* CLUVAC PCLUS3-18IIIB (SEQ ID NO:2).

25. (Amended) A method for inducing a [protective] an antigen specific systemic and rectal mucosal CTL response in a mammalian subject, comprising contacting a rectal mucosal tissue of the subject with a composition comprising a [soluble antigen] chimeric peptide containing a subregion with multiple overlapping helper T cell activating epitopes of a HIV isolate that can be presented by multiple MHC class II molecules and a subregion with a CTL activating epitope of the HIV isolate, wherein said composition does not comprise an adjuvant, and wherein the contacting induces an antigen specific systemic and rectal mucosal cytotoxic T lymphocyte response that can reduce the replication of a virus expressing the CTL activating epitopes of the HIV isolate.

27. (Amended) The method of claim 26, wherein the cytokine is contacted with [a] the rectal mucosal surface of the subject.

42. (Amended) The method of claim 25, wherein the [antigen is a] chimeric peptide [comprising an *HIV-1* cluster peptide vaccine construct (CLUVAC) selected from the group consisting of] comprises:

EQMHEDIISLWDQSLKPCVKRIQRGPGRAFVTIGK (SEQ ID NO.: 1)

KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK (SEQ ID NO: 2)

RDNWRSELYKYKVVKIEPLGVAPTRIQRGPGRAFVTIGK (SEQ ID NO: 3)

AVAEGTDVIEVVQGAYRAIRHIPRRIRQGLERRIQRGPGRAFVTIGK (SEQ ID NO: 4),

DRVIEVVQGAYRAIRHIPRRIRQGLERRIQRGPGRAFVTIGK (SEQ ID NO: 5),

DRVIEVVQGAYRAIRRIQRGPGRAFVTIGK (SEQ ID NO: 6),

AQGAYRAIRHIPRRIRRIQRGPGRAFVTIGK (SEQ ID NO: 7),

EQMHEDIISLWDQSLKPCVKRIRIHIGPGRAFYTTKN (SEQ ID NO: 8),

KQIINMWQEVGKAMYAPPISGQIRRIHIGPGRAFYTTKN (SEQ ID NO: 9),

RDNWRSELYKYKVVKIEPLGVAPTRIHIGPGRAFYTTKN (SEQ ID NO: 10),

AVAEGTDVIEVVQGAYRAIRHIPRRIRQGLERRIHIGPGRAFYTTKN (SEQ ID NO: 11),

DRVIEVVQGAYRAIRHIPRRIRQGLERRIHIGPGRAFYTTKN (SEQ ID NO: 12),

DRVIEVVQGAYRAIRRIHIGPGRAFYTTKN (SEQ ID NO: 13), or

AQGAYRAIRHIPRRIRRIHIGPGRAFYTTKN (SEQ ID NO: 14).

43. (Amended) The method of claim 42, wherein the [*HIV-1* CLUVAC] chimeric peptide is *HIV-1* CLUVAC PCLUS3-18IIIB (SEQ ID NO:2).

46. (Amended) An immunogenic composition [for inducing a protective mucosal CTL response in a subject and] comprising a chimeric peptide containing a subregion

with multiple overlapping helper T cell activating epitopes from an HIV isolate that can be presented by multiple MHC class II molecules and a subregion with a CTL activating epitope from the HIV isolate, [adapted for intrarectal administration comprising a purified soluble antigen] formulated for intrarectal delivery to the rectum, colon, sigmoid colon, or distal colon that induces an antigen specific systemic and rectal mucosal cytotoxic T cell response that can kill or reduce the proliferation of a virus expressing the cytotoxic T cell epitope.

49. (Amended) The immunogenic composition of claim 48, [which includes] formulated as a rectal emulsion or gel preparation.

50. (Amended) The immunogenic composition of claim 48, wherein the [soluble antigen] chimeric peptide is admixed with a homogeneous gel carrier.

51. (Amended) The immunogenic composition of claim [48] 50, wherein the homogeneous gel carrier is a polyoxyethylene gel.

52. (Amended) The immunogenic composition of claim 48, wherein the [soluble antigen] chimeric peptide is admixed with a rectally-compatible foam.

53. (Amended) The immunogenic composition of claim 48, wherein the [soluble antigen] chimeric peptide is formulated in a suppository.

55. (Amended) The immunogenic composition of claim [53] 54, comprising at least two base materials.

56. (Amended) The immunogenic composition of claim 46, including a stabilizing agent to minimize intrarectal degradation of the [soluble antigen] chimeric peptide.

57. (Amended) The immunogenic composition of claim 46, [including] further comprising an absorption-promoting agent.